

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/012279

International filing date (day/month/year)
29.10.2004

Priority date (day/month/year)
18.11.2003

International Patent Classification (IPC) or both national classification and IPC
C07F9/6568

Applicant
DEGUSSA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Elliott, A

Telephone No. +49 89 2399-8218



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/EP2004/012279

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/012279

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-13
	No: Claims	-
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-13
	No: Claims	-

2. Citations and explanations

see separate sheet

The following documents will be referred to in this opinion:

- D1: WO 03/084971 A (DEGUSSA) 16 October 2003 (2003-10-16)
- D2: WO 91/17998 A (DU PONT) 28 November 1991 (1991-11-28)
- D3: WO 99/24444 A (CHIROTECH TECHNOLOGY LTD) 20 May 1999 (1999-05-20)
- D4: PILKINGTON C J ET AL: "Expanding the Family of Phospholane-Based Ligands: 1,2-Bis(2,5-diphenylphospholano)ethane" ORGANIC LETTERS, ACS, WASHINGTON, DC, US, vol. 5, no. 8, 17 April 2003 (2003-04-17), pages 1273-1275, XP002301264 ISSN: 1523-7060
- D5: HOLZ J ET AL: "Synthesis of a New Chiral Bisphospholane Ligand for the Rh(I)-Catalyzed Enantioselective Hydrogenation of Isomeric beta-Acylamido Acrylates" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON, US, vol. 68, no. 5, 12 February 2003 (2003-02-12), pages 1701-1707, XP002244188 ISSN: 0022-3263
- D6: BURK M J: "New chiral phospholanes; synthesis, characterization, and use in asymmetric hydrogenation reactions" TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 2, no. 7, 1991, pages 569-592, XP002146730 ISSN: 0957-4166
- D7: BLOOMFIELD P R ET AL: "Direct preparation of phenylphosphine dilithium" CHEMISTRY AND INDUSTRY, 25 April 1959 (1959-04-25), pages 541-542, XP009005175 ISSN: 0009-3068
- D8: YAN Y-Y ET AL: "Highly Flexible Synthetic Routes to Functionalized Phospholanes from Carbohydrates" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON, US, vol. 65, 11 February 2000 (2000-02-11), pages 900-906, XP002233658 ISSN: 0022-3263
- D9: NANDI M ET AL: "Synergistic effects of hemilabile coordination and counterions in homogeneous catalysis: new turnable monophosphine ligands for hydrovinylolation reactions" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 121, no. 42, 27 October 1999 (1999-10-27), pages 9899-9900, XP002316158 ISSN: 0002-7863
- D10: BRAUER D J ET AL: "Novel P,N ligands derived from (R)- and (S)-1-phenylethylamine with (2R,5R)-2,5-dimethylphospholanyl groups (DuPHAMIN) for asymmetric catalysis" EUROPEAN JOURNAL OF INORGANIC CHEMISTRY, no. 9, May 2003 (2003-05), pages 1748-1755, XP002316159 ISSN: 1434-1948
- D11: LI W ET AL: "Synthesis of chiral hydroxyl phospholanes from D-mannitol and their use in asymmetric catalytic reactions" JOURNAL OF ORGANIC CHEMISTRY, vol. 65, no. 11, 2 June 2000 (2000-06-02), pages 3489-3496, XP002316160 ISSN: 0022-3263

Re Item V.

The subject-matter of the application would appear new in the light of the slight difference in the way in which the phospholanes according to formula (I) are prepared in the prior art which can be seen in the characterising portion of claim 1, namely in the way in which the intermediate (II) is produced whereby compound (IV) is reacted with compound (V) to prepare (II) with (IV) being prepared by the reaction of (VI) ($\text{Hal}_2\text{P-Aryl}$) with an alkali metal.

However, said same subject-matter would appear to be devoid of an inventive step on the following grounds:

A number of documents can be regarded as closest prior art as they disclose methods of

preparing compounds according to formula (I). The difference between these known processes and that presently-claimed lies in the start of the preparation process where the Li_2PPh is prepared (in D1 on page 13 this is said to be by the method of D9 (scheme 1) where PhPH_2 is reacted with an alkali metal; D2, cf. Scheme I on page 8 - here how the Li_2PPh is prepared is not given; D5, cf. Scheme 1 where PhPH_2 is used; D6, scheme I on page 571 - again how the Li_2PPh was made is not given). D8-D11 give similar processes starting always from aryl- PH_2 compounds.

The object of the present application is to be seen in the provision of an alternative route for preparing bisphospholanes with an unsaturated bridge between the two phospholanes.

The solution according to claim 1 has been to synthesise the Li_2PPh differently in that it is synthesised not from PhPH_2 but from Hal P-aryl . An inventive step cannot be acknowledged because document D7 from 1959 shows this very process. Hence claims 1-13 are seen to lack an inventive step on the grounds that an alternative known preparation methods has been employed for one of the starting materials already known from the prior art.